THE ALKALOIDS

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PREFACE

The literature dealing with alkaloids shows no obvious signs of abatement. The classic methods of the organic chemist employed in structural determinations have evolved into spectral methods, and chemical reactions are involved largely in confirmatory and periferal studies. Inasmuch as the spectral methods have become largely standardized we incline to limit the details in these volumes.

Many new and already known alkaloids have been isolated from new and from previously examined sources. Novel syntheses are a prominent feature of recent publications. We attempt to review timely topics related to alkaloids.

R. H. F. MANSKE

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——CHAPTER 1——

THE ERGOT ALKALOIDS

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I. Introduction

The chemistry of the ergot alkaloids was last reviewed in Volume VIII of this treatise (*1*). A remarkable monograph appeared in 1964 covering in brief all the achievements in ergot chemistry to that time (*2*).

Ergot research of the past 10 years may be characterized as a harvesting period of intensive previous investigations. Relatively few new alkaloids have been described in the meantime, most of them being only of biogenetic significance. They all originate from parasitic fungi although certain ergot alkaloids have been known to occur also in higher plants, especially in Convolvulaceae (*1*).

Recent progress lies mainly in the field of synthesis. Extensive work has also been done in order to gain more information about biosynthesis. It must however be emphasized that the mechanism of important biochemical transformations still remains obscure.

II. New Alkaloids

A. Introduction

Since the last review on ergot alkaloids, important new alkaloids from different sources, mostly from new ergot strains, have been discovered. Their proposed structure could in some cases be confirmed by synthesis. Some of them seem to be intermediates in the biogenetic pathway from tryptophan to the peptide alkaloids. Others are considered as end products of secondary plant metabolism. In any case we find many interesting structures among these recently discovered substances.

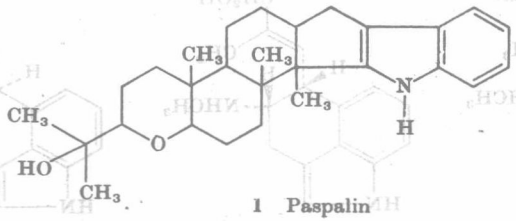
B. Paspalin and Paspalicin

From the dried mycel of a Portuguese *Claviceps paspali* strain, two new indole derivatives, paspalin (**1**; $C_{28}H_{39}NO_2$; mp 264°; $[\alpha]_D$ −23° in chloroform) and paspalicin (**2**; $C_{27}H_{31}NO_3$; mp ~ 230°; $[\alpha]_D$ +173° in chloroform) were isolated (*3*).

1. Paspalin

Structure **1** had been proposed for paspalin, based mainly on biogenetic speculations (*124*). Extensive degradative work (*125*) has now confirmed this, although its stereochemistry has yet to be elucidated.

Paspalin cannot be regarded as a true alkaloid, its unique structure—a seco-steroid annelated to an indole nucleus—deserves, however, attention as it demonstrates the great versatility of the ergot fungus.



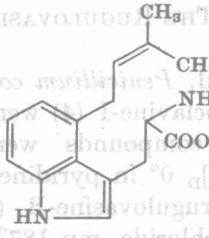
1 Paspalin

2. Paspalicin

Less is known about paspalicin. It is also regarded as a 2,3-disubstituted indole derivative with four tertiary methyl groups and probably an α,β-unsaturated carbonyl group.

C. 4-Dimethylallyltryptophan

4-Dimethylallyltryptophan (**3**; $C_{16}H_{20}N_2O_2$; mp 210°) had already been synthesized in 1963 (*4*) and shortly afterward it was recognized as an important intermediate in biosynthesis of ergot alkaloids (*5*).

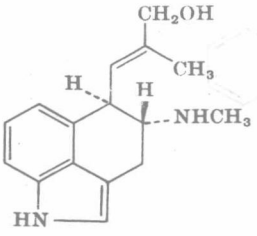


3 4-Dimethylallyltryptophan

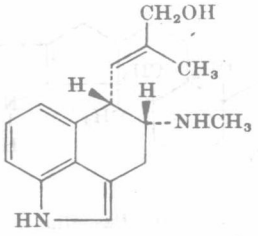
In 1968 the existence of **3** in a *Pennisetum* type of ergot strain, producing mainly elymoclavine, could be established after addition of ethionine to the culture broth (*6*).

D. The Chanoclavines

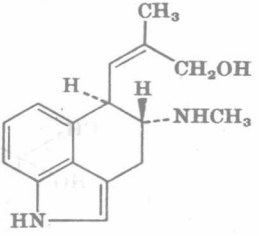
In 1964, two new isomers of the known chanoclavine-I (*7*) were isolated from the water-soluble fraction of Portuguese rye ergot (*8*). Interpretation of the physical data, essentially of the NMR spectra, permitted the establishment of the stereochemistry of these three isomers.



4 Chanoclavine-I



5 Chanoclavine-II



6 Isochanoclavine-I

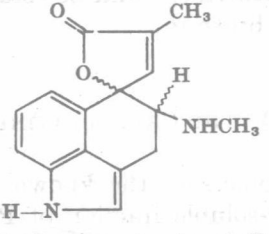
The stereoformula **4** could be assigned to chanoclavine-I ($C_{16}H_{20}N_2O$; mp 220°; $[\alpha]_D$ −294° in pyridine).

Chanoclavine-II (**5**; $C_{16}H_{20}N_2O$; mp 174°; $[\alpha]_D$ −332° in pyridine; hydrochloride, mp 247°) differs from **4** only in the *cis* configuration of the substituents on ring C. Its absolute configuration could not be fixed, however; so far the formula **5** is tentative. The isolated optically active isomer of **5** was also accompanied by the racemic form.

The third isomer, isochanoclavine-I ($C_{16}H_{20}N_2O$; mp 181°; $[\alpha]_D$ −216° in pyridine), is represented by formula **6**. It differs from **4** in the position of the substituents on the isolated double bond.

E. The Rugulovasines

From cultures of a mold, *Penicillium concavo-rugulosum*, two new alkaloids as well as chanoclavine-I (**4**) were isolated by routine procedures (*9*). The new compounds were called rugulovasine-A ($C_{16}H_{16}N_2O_2$; mp 138°; $[\alpha]_D$ 0° in pyridine; hydrochloride, mp 225°; oxalate, mp 224°) and rugulovasine-B ($C_{16}H_{16}N_2O_2$; amorphous; $[\alpha]_D$ 0° in pyridine; hydrochloride, mp 187°; oxalate, mp 217°). They proved to be closely related to each other since they were easily interconvertible when heated in alcohol solution.



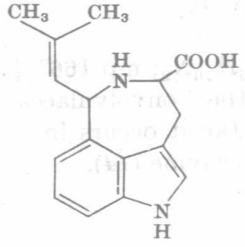
7 Rugulovasine-A and -B

The accumulated information from the physical data and some

chemical transformations (*10*) led to the tentative formula **7** for rugulovasine-A and -B. The steric details remain to be elucidated.

F. Clavicipitic Acid

From the culture filtrates of two different *Claviceps* species, strain SD 58 and *C. fusiformis*, strain 139/2/1G, a new amino acid was isolated, named clavicipitic acid, ($C_{16}H_{18}N_2O_2$; mp 262°).



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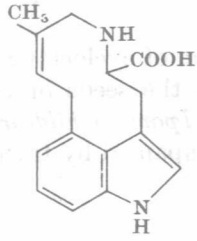

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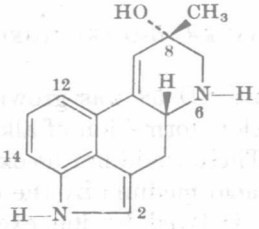
Formula **9** proposed at first (*11*) was based mainly on mass spectral data (M^+) and biosynthetic evidence since only small quantities of the new amino acid were available. Very recently, however, its structure has been revised (*12*) to **8**, mainly on NMR studies of its crystalline *N*-acetylmethyl ester derivative (mp 107°; M^+ 326). The observed two three-proton singlets at 1.68 and 1.82 ppm ($CDCl_3$) are inconsistent with formula **9**.

G. 6-Norsetoclavine

In the culture filtrates of two *Pennisetum* ergot strains 47A and 231 the first representative of 6-norclavine alkaloids was found (*13*) and identified as 6-norsetoclavine (**10**; $C_{15}H_{16}N_2O$; mp 163–165°).



10 6-Norsetoclavine